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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,513	10/24/2005	Gerald Wayne Both	64162-032	2743

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EXAMINER	
KELLY, ROBERT M	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
09/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,513	BOTH ET AL.	
	Examiner	Art Unit	
	Robert M. Kelly	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/28/06; 9/28/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-28 are presently pending and considered.

Information Disclosure Statement

It is noted that the 12/28/06 IDS contains a duplicated reference (Voeks, et al.) from the IDS of 9/28/04. As such, while it has been initialed, the second reference has been crossed off and marked as a duplicate to indicate such, so that it is not reprinted twice on any patent that may issue.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-57 of U.S. Patent No. 7,019,030 to Setiawan,

and/or claims 1-51 of US Patent No. 6,020,172 to Both and/or claims 1-18 of U.S. Patent No. 7,037,712 to Both, separately and/or in combination, and further in view of U.S. Patent No. 6,159,467 to Chung, et al., and Khatri, et al. (1997) Virology, 239: 226-37, as further evidenced by Lee, et al. (2000) Cancer Gene Therapy, 7(10): 1329-35; Ryuke, et al. (2000) Neurol. Med. Chir. (Tokyo) 40: 256-60; Ma, et al. (2002) Gene Therapy, 9: 176-82; Dunphy, et al. (1999) Human Gene Therapy, 10: 2407-17; Sung, et al. (2000) Anticancer Research, 20(3A): 1653-66; Meunier-Durmort, et al. (1996) European Journal of Biochemistry, 237: 660-67; and Natsume, et al. (2000) Japanese Journal of Cancer Research, 91(4): 363-67), Qiu, et al. (1998) Human Gene Therapy, 9(4): 507-20 (ABSTRACT ONLY); and Hodgeson (1996) Nature Biotechnology, 14: 339-342; Song, et al. (2000) Oncology Reports, 7(1): 119-24; Porter, et al. (1998) Journal of Virology, 72(6): 4832-40; Saeki, et al. (1997) Human Gene Therapy, 8(17): 2133-41; Kaneko, et al. (1996) Cancer Letters 107: 211-15; Kaneko, et al. (1996) Cancer Letters, 105: 39-44; Shimura, et al. (1985) Virology, 144(1): 268-72, and further in view of Martiniello-Wilks, et al. (1998) Human Gene Therapy, 9(11): 1617-26 (ABSTRACT ONLY), and further in view of U.S. Patent No. 6,197,293 to Henderson, et al.

The Setiawan patent is drawn to atadenoviruses, including OAV623, and further a composition of a cationic lipid, which may be CSO87, or members of the genera including CSO60. The patent teaches that these lipids may be used as a cyroprotectant, however, the Art above, teaches the other aspects of the claims, as is shown throughout the Art rejections, below.

The Both '172 patent teaches and claims ovine adenoviruses, the prodrug/enzyme combinations claimed, the promoters claimed, and the use of chimeric fiber proteins, to, *inter alia*, treat cancers.

The Both '712 patent teaches and claims the generic atadenoviruses and the OAV287 atadenovirus which is the prototype upon which all other modifications are made in the art.

Hence, in light of any single patent and/or any combination of the patents, and further in view of the Art cited, it would have been obvious to make the claimed inventions. The Artisan would have found it simple substitution of one structure for an equivalent one, thereby producing predictable results.

Claim Rejections - 35 USC § 112 – enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for direct administration to the tumor, does not reasonably provide enablement for any form of administration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant's claims encompass any form of administration to transform cancer cells in a subject, and thereby express a suicide gene which converts a subsequently administered prodrug, thereby killing the cancer cells.

The problem of targeting the tissue is one of the biggest problems in the Art with regard to therapeutics in gene therapy techniques. With regard to gene therapy, while progress has been made in recent years for gene transfer *in vivo*, vector targeting to desired tissues *in vivo*

continues to be a difficulty as supported by numerous teachings available in the art. For example, Deonarain (1998) Expert Opin. Ther. Pat., 8: 53-69, indicates that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequeate levels for a long enough period of time" (p. 53, first paragraph). Deonarain reviews new techniques under experimentation in the art which show promise but states that such techniques are even less efficient than viral gene delivery (p. 65, CONCLUSION). Verma (1997) Nature, 389: 239-242, reviews vectors known in the art for use in gene therapy and discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (entire article). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (p. 240, sentence bridging columns 2 and 3). Verma states that "The Achilles heel of gene therapy is gene delivery and this is the aspect we will concentrate on here. Thus far, the problem has been an inability to deliver genes efficiently and to obtain sustained expression ... The use of viruses (viral vectors) is a powerful technique, because many of them have evolved a specific machinery to deliver DNA to cells. However, humans have an immune system to fight off the virus, and our attempts to deliver genes in viral vectors have been confronted by these host responses (e.g., p. 239, col. 3).

Further, Eck et al. (1996) Goodman & Gilman's The Pharmacological Basis of Therapeutics, McGraw-Hill, New York, NY., pp. 77-101, states that the fate of the DNA vector itself (volume of distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, and the rate of

degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced, are all important factors for a successful gene therapy (e.g., bridging pp. 81-82). In addition, Gorecki (2001) Expert Opin. Emerging Drugs 6(2): 187-98) reports that "the choice of vectors and delivery routes depends on the nature of the target cells and the required levels and stability of expression" for gene therapy, and obstacles to gene therapy *in vivo* include "the development of effective clinical products" and "the low levels and stability of expression and immune responses to vectors and/or gene products" (e.g., ABSTRACT).

Still further, in the case of the liposome co-administered, the adenovirus will have even better tropism for many tissues (e.g., Lee, et al. (2000) Cancer Gene Therapy, 7(10): 1329-35; Ryuke, et al. (2000) Neurol. Med. Chir. (Tokyo) 40: 256-60; Ma, et al. (2002) Gene Therapy, 9: 176-82; Dunphy, et al. (1999) Human Gene Therapy, 10: 2407-17; Sung, et al. (2000) Anticancer Research, 20(3A): 1653-66; Meunier-Durmort, et al. (1996) European Journal of Biochemistry, 237: 660-67; and Natsume, et al. (2000) Japanese Journal of Cancer Research, 91(4): 363-67) and hence, if not directly administered, the viruses would be predicted to transform many other cell tissues before even reaching the target tumor tissue, and therefore, the prodrug would kill distinct tissues and possibly even the subject, before therapy is even affected.

Applicant's specification provides evidence of increased transformation efficiency (EXAMPLES) however, there is no specific direction, guidance or examples, which would allow the Artisan to reasonably predict that any particular form of administration, besides direct

administration would allow for specific targeting of tumor tissues, allowing enough protein to be produced, and not killing off other tissues.

Hence, outside of direct administration, the Artisan would not reasonably predict any other form of administration would be efficacious. Hence, the Artisan would have to experiment with the other forms of administration in any particular cancer and subject to determine which forms of administration would affect therapy without killing the patient. Such experimentation is undue because it amounts to inventing the breadth of Applicant's claimed invention for Applicant.

Hence, the claims are not enabled for any form of administration besides direct administration to the tissue. The composition claims are included in the rejection, as they are commensurate with the method claims and as such, it is apparent that they must be enabled for the same scope.

Note: Rejections on Art – It is noted that the rejections are based on new office policy in light of KSR v. Teleflex, 550 US --, 82 USPQ.2d 1385 (2007), which it is recommended is reviewed prior to responding to the rejections herein

Rejections on basic method/compositions

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 9, 10, 12-14, 16, 17, 22, 23, and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,159,467 to Chung, et al., and Khatri, et al. (1997) Virology, 239: 226-37, as further evidenced by Lee, et al. (2000) Cancer Gene Therapy, 7(10): 1329-35; Ryuke, et al. (2000) Neurol. Med. Chir. (Tokyo) 40: 256-60; Ma, et al. (2002) Gene Therapy, 9: 176-82; Dunphy, et al. (1999) Human Gene Therapy, 10: 2407-17; Sung, et al. (2000) Anticancer Research, 20(3A): 1653-66; Meunier-Durmort, et al. (1996) European Journal of Biochemistry, 237: 660-67; and Natsume, et al. (2000) Japanese Journal of Cancer Research, 91(4): 363-67, Qiu, et al. (1998) Human Gene Therapy, 9(4): 507-20 (ABSTRACT ONLY); and Hodgeson (1996) Nature Biotechnology, 14: 339-342; Song, et al. (2000) Oncology Reports, 7(1): 119-24; Porter, et al. (1998) Journal of Virology, 72(6): 4832-40; Saeki, et al. (1997) Human Gene Therapy, 8(17): 2133-41; Kaneko, et al. (1996) Cancer Letters 107: 211-15; Kaneko, et al. (1996) Cancer Letters, 105: 39-44; Shimura, et al. (1985) Virology, 144(1): 268-72, and as further evidenced by U.S. Patent No. 7,091,030 to Setiawan.

Chung teaches the use of recombinant adenovirus vectors comprising a promoter operatively to a thymidine kinase encoding region, for suicide gene therapy of, *inter alia*, prostate cancer, and several other forms of cancer (e.g., ABSTRACT). Chung teaches direct administration of such vectors to the cancer (ABSTRACT), which may be a solid tumor (e.g., cols. 2-3, paragraph bridging). However, Chung does not teach the use of Ovine (atadenovirus) vectors.

On the other hand, Khatri teaches that the Ovine Adenovirus prototype, OAV287, can infect many human cell cancer types, including at least one prostate cancer (e.g., ABSTRACT).

However, neither Khatri nor Chung teach the further use of cationic lipids in the composition for administration.

On the other hand, a wide range of art on adenoviruses at the time of invention taught that the use of cationic liposomes would increase the transfection efficiency of adenoviruses (e.g., Lee, et al. (2000) Cancer Gene Therapy, 7(10): 1329-35; Ryuke, et al. (2000) Neurol. Med. Chir. (Tokyo) 40: 256-60; Ma, et al. (2002) Gene Therapy, 9: 176-82; Dunphy, et al. (1999) Human Gene Therapy, 10: 2407-17; Sung, et al. (2000) Anticancer Research, 20(3A): 1653-66; Meunier-Durmort, et al. (1996) European Journal of Biochemistry, 237: 660-67; and Natsume, et al. (2000) Japanese Journal of Cancer Research, 91(4): 363-67). Furthermore, such enhancement is distinct from the fiber receptor and alpha(v) integrin pathways of entry (e.g., Qiu, et al. (1998) Human Gene Therapy, 9(4): 507-20 (ABSTRACT ONLY)).

Moreover, a wider range of art demonstrates that the effect of cationic liposomes to enhance transfection efficiency of viral vector particles goes far beyond adenovirus vectors (e.g., Hodgeson (1996) Nature Biotechnology, 14: 339-342; Song, et al. (2000) Oncology Reports, 7(1): 119-24; Porter, et al. (1998) Journal of Virology, 72(6): 4832-40; Saeki, et al. (1997) Human Gene Therapy, 8(17): 2133-41; Kaneko, et al. (1996) Cancer Letters 107: 211-15; Kaneko, et al. (1996) Cancer Letters, 105: 39-44; Shimura, et al. (1985) Virology, 144(1): 268-72).

Still further, Setiawan teaches the specific CSO 87 (e.g., CLAIMS), as well all the genera to which CSO 60 belongs, as cationic lipids.

Hence, all of the elements were known in the prior art for transforming solid cancers, including pancreatic cancer. Thus it would have been obvious to the Artisan to use an ovine

adenovirus to deliver the TK gene to a solid tumor, in the presence of cationic liposomes, since the references teach that Ovine adenoviruses could transform many types of human cancer cells, and that cationic liposomes could enhance the transformation of cells using many virus particle types, and specifically adenoviral vectors. Hence, the combination would achieve the predictable result of transforming the cells, and further administration of the prodrug acyclovir, as taught in Chung, and thereby kill the cancer cells.

Further, Chung teaches tissue-specific promoters (e.g., cols. 2-3, paragraph bridging).

Further, with regard to the specific lipids claimed, the Artisan would instantly recognize that any cationic lipid could be used, given the confluence of the Art demonstrating effect.

With regard to the compositions in general, as the methods are taught, the compositions are necessarily obvious. Further, the compositions are necessarily also obvious without the requirement for increased transfection efficiency, as Setiawan teaches the compositions would stabilized by the presence of the lipids.

Art Rejections Substituting PNP/6MPDR for TK/acyclovir combinations

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 9-14, 16, 17, and 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,159,467 to Chung, et al., and Khatri, et al. (1997) Virology,

239: 226-37, as further evidenced by Lee, et al. (2000) Cancer Gene Therapy, 7(10): 1329-35; Ryuke, et al. (2000) Neurol. Med. Chir. (Tokyo) 40: 256-60; Ma, et al. (2002) Gene Therapy, 9: 176-82; Dunphy, et al. (1999) Human Gene Therapy, 10: 2407-17; Sung, et al. (2000) Anticancer Research, 20(3A): 1653-66; Meunier-Durmort, et al. (1996) European Journal of Biochemistry, 237: 660-67; and Natsume, et al. (2000) Japanese Journal of Cancer Research, 91(4): 363-67), Qiu, et al. (1998) Human Gene Therapy, 9(4): 507-20 (ABSTRACT ONLY); and Hodgeson (1996) Nature Biotechnology, 14: 339-342; Song, et al. (2000) Oncology Reports, 7(1): 119-24; Porter, et al. (1998) Journal of Virology, 72(6): 4832-40; Saeki, et al. (1997) Human Gene Therapy, 8(17): 2133-41; Kaneko, et al. (1996) Cancer Letters 107: 211-15; Kaneko, et al. (1996) Cancer Letters, 105: 39-44; Shimura, et al. (1985) Virology, 144(1): 268-72 and as further evidenced by U.S. Patent No. 7,091,030 to Setiawan, as applied to claims 1-4, 9, 10, 12-14, 16, 17, 22, 23, and 25-27 above, and further in view of Martiniello-Wilks, et al. (1998) Human Gene Therapy, 9(11): 1617-26 (ABSTRACT ONLY).

As shown above, the references teach the aspects rejected, however, they do not teach the use of PNP and 6MPDR.

However, Martiniello-Wilks teaches the use of PNP/6MPDR in similar methods of treating cancer cells, including prostate cancer cells.

Hence, at the time of invention, it would have been obvious to further modify the invention above to use the PNP/6MPDR of Martiniello-Wilks. Because both references teach equivalent mechanisms of suicide gene therapy, it would be obvious to the Artisan to substitute one gene/prodrug with another, with the predictable result of killing cancer cells.

Art Rejections Further Comprising an AdV type 5 Fiber

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 9-14, 16, 17, and 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,159,467 to Chung, et al., and Khatri, et al. (1997) Virology, 239: 226-37, as further evidenced by Lee, et al. (2000) Cancer Gene Therapy, 7(10): 1329-35; Ryuke, et al. (2000) Neurol. Med. Chir. (Tokyo) 40: 256-60; Ma, et al. (2002) Gene Therapy, 9: 176-82; Dunphy, et al. (1999) Human Gene Therapy, 10: 2407-17; Sung, et al. (2000) Anticancer Research, 20(3A): 1653-66; Meunier-Durmort, et al. (1996) European Journal of Biochemistry, 237: 660-67; and Natsume, et al. (2000) Japanese Journal of Cancer Research, 91(4): 363-67), Qui, et al. (1998) Human Gene Therapy, 9(4): 507-20 (ABSTRACT ONLY); and Hodgeson (1996) Nature Biotechnology, 14: 339-342; Song, et al. (2000) Oncology Reports, 7(1): 119-24; Porter, et al. (1998) Journal of Virology, 72(6): 4832-40; Saeki, et al. (1997) Human Gene Therapy, 8(17): 2133-41; Kaneko, et al. (1996) Cancer Letters 107: 211-15; Kaneko, et al. (1996) Cancer Letters, 105: 39-44; Shimura, et al. (1985) Virology, 144(1): 268-72, as applied to claims 1-4, 9, 10, 12, 16, 17, 22, 23, and 25 above, and further in view of Martiniello-Wilks, et al. (1998) Human Gene Therapy, 9(11): 1617-26 (ABSTRACT ONLY), and as further evidenced by U.S. Patent No. 7,091,030 to Setiawan as applied to claims 1-4, 9-14, 16, 17, and 22-27 above, and further in view of Xu, et al. (1998) Virology, 248: 156-63.

As shown above, the various references obviate the claims cited, however, the Artisan would be further find it obvious to modify the references by using the Ovine adenovirus of Xu, containing the cell-binding domain of a human type 5 adenovirus. The Artisan would be motivated to do so increase the breadth of prostate cancer types that could be transformed by the virus, as taught by Xu (ABSTRACT). Moreover, the Artisan would have had a reasonable expectation of success, as Xu had demonstrated that the modified virus would also transform LnCaP prostate cancer cells with increased efficiency.

Art Rejections Utilizing the Probasin Promoter and/or PSA Enhancer

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-14 and 16-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,159,467 to Chung, et al., and Khatri, et al. (1997) Virology, 239: 226-37, as further evidenced by Lee, et al. (2000) Cancer Gene Therapy, 7(10): 1329-35; Ryuke, et al. (2000) Neurol. Med. Chir. (Tokyo) 40: 256-60; Ma, et al. (2002) Gene Therapy, 9: 176-82; Dunphy, et al. (1999) Human Gene Therapy, 10: 2407-17; Sung, et al. (2000) Anticancer Research, 20(3A): 1653-66; Meunier-Durmort, et al. (1996) European Journal of Biochemistry, 237: 660-67; and Natsume, et al. (2000) Japanese Journal of Cancer Research, 91(4): 363-67), Qui, et al. (1998) Human Gene Therapy, 9(4): 507-20 (ABSTRACT ONLY); and Hodgeson

(1996) Nature Biotechnology, 14: 339-342; Song, et al. (2000) Oncology Reports, 7(1): 119-24; Porter, et al. (1998) Journal of Virology, 72(6): 4832-40; Saeki, et al. (1997) Human Gene Therapy, 8(17): 2133-41; Kaneko, et al. (1996) Cancer Letters 107: 211-15; Kaneko, et al. (1996) Cancer Letters, 105: 39-44; Shimura, et al. (1985) Virology, 144(1): 268-72, and further in view of Martiniello-Wilks, et al. (1998) Human Gene Therapy, 9(11): 1617-26 (ABSTRACT ONLY), and as further evidenced by U.S. Patent No. 7,091,030 to Setiawan as applied to claims 1-4, 9-14, 16, 17, and 22-27 above, and further in view of U.S. Patent No. 6,197,293 to Henderson, et al.

Also:

Claims 1-14 and 16-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,159,467 to Chung, et al., and Khatri, et al. (1997) Virology, 239: 226-37, as further evidenced by Lee, et al. (2000) Cancer Gene Therapy, 7(10): 1329-35; Ryuke, et al. (2000) Neurol. Med. Chir. (Tokyo) 40: 256-60; Ma, et al. (2002) Gene Therapy, 9: 176-82; Dunphy, et al. (1999) Human Gene Therapy, 10: 2407-17; Sung, et al. (2000) Anticancer Research, 20(3A): 1653-66; Meunier-Durmort, et al. (1996) European Journal of Biochemistry, 237: 660-67; and Natsume, et al. (2000) Japanese Journal of Cancer Research, 91(4): 363-67), Qui, et al. (1998) Human Gene Therapy, 9(4): 507-20 (ABSTRACT ONLY); and Hodgeson (1996) Nature Biotechnology, 14: 339-342; Song, et al. (2000) Oncology Reports, 7(1): 119-24; Porter, et al. (1998) Journal of Virology, 72(6): 4832-40; Saeki, et al. (1997) Human Gene Therapy, 8(17): 2133-41; Kaneko, et al. (1996) Cancer Letters 107: 211-15; Kaneko, et al. (1996) Cancer Letters, 105: 39-44; Shimura, et al. (1985) Virology, 144(1): 268-72, and further

in view of Martiniello-Wilks, et al. (1998) Human Gene Therapy, 9(11): 1617-26 (ABSTRACT ONLY), and further in view of Xu, et al. (1998) Virology, 248: 156-63 and as further evidenced by U.S. Patent No. 7,091,030 to Setiawan as applied to claims 1-4, 9-14, 16, 17, and 22-27 above, and further in view of U.S. Patent No. 6,197,293 to Henderson, et al.

As noted above, the references make obvious the various claimed limitations, except for the use of the probasin promoter and the prostate-specific antigen enhancer.

On the other hand, Henderson teaches one such specific promoter and enhancer combination which exerts prostate specific expression (e.g., ABSTRACT), comprises a prostate-specific antigen enhancer and a probasin promoter (e.g., col. 8, paragraph 3).

Hence, it would be obvious to modify the invention to use a promoter from the probasin gene and/or the enhancer of the prostate specific antigen gene. It would be obvious to the Artisan to substitute one promoter/enhancer for another in order to achieve the predictable result of expressing the suicide gene in prostate cancer cells and thereby kill the cells.

Art Rejections of Specific Virus Claims

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 9-15, 16-17, and 22-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of the above-listed rejections as applied to those claims applicable to each above, and further in view of Pramudji, et al. (2001) Clinical Cancer Research, 7: 4272-79, Krohne, et al. (2001) Hepatology, 34: 511-18, and Ramasamy, et al. (1999) Biochimica et Biophysica Acta, 1453: 1-13.

With regard to the various subject matter claimed, those claims that are obvious in the above-listed rejections are similarly obvious here.

However, the cited art does not teach the use of OADV 220, 223, or 623. On the other hand, OADV 220 is simply modified to comprise the RSV promoter, PNP encoding sequence, and BGH polyA tail between PIII and Fiber sequences of the OAV 287, above.

On the other hand, Pramudji teaches the use of the RSV promoter sequence to express proteins in prostate cancer cells (ABSTRACT), Krohne teaches the use of PNP encoding sequences to kill cancer cells (ABSTRACT), and Ramasamy teaches the use of BGH polyA sequences to terminate translation in eukaryotic cells (e.g., ABSTRACT). Such are the same sequences that Applicant uses to make the OAV220 claimed.

Hence, as the promoter, encoding region, and polyA sequence was known in the Art, it would have been obvious to the Artisan to substitute these sequences for the other sequences, as they each would achieve the equivalent function of expression, production of a PNP, and termination of translation, in predictable fashion. In addition, the choice of where in the virus to place the sequence, and exact sequences used are simply one of design choice and would not affect the function therein. Hence, the OAV220 is obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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